THE ORIENTATION OF THE NITRO-GROUP IN NITROMYRISTICINIC ACID

BY

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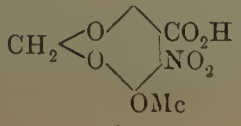
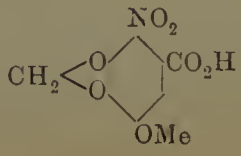
XXXII.—*The Orientation of the Nitro-Group in Nitromyristicinic Acid.*

By Arthur Henry Salway.

In a previous investigation (Trans., 1909, **95**, 1165) it was shown that myristicinic acid is converted by the action of cold concentrated nitric acid into a mixture of 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene and nitromyristicinic acid. The position of the nitro-group in the latter compound was not definitely established, there being two possible formulæ, as represented by I and II:



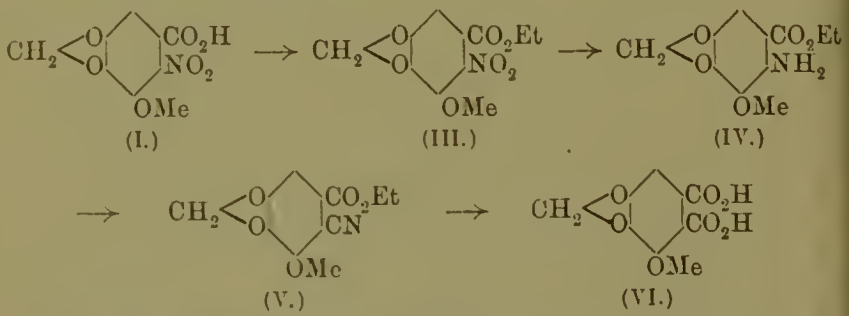
(I.)



(II.)

The present investigation was therefore undertaken with the object of ascertaining which of these formulæ must be assigned to the nitromyristicinic acid prepared in the above-mentioned reaction.

The method employed consisted in the conversion of the nitro-group of nitromyristicinic acid into a carboxylic group, when the product would be cotarnic acid (VI) or an isomeride, according as the constitution of nitromyristicinic acid is represented by formula I or II. This transformation was successfully accomplished according to the series of reactions represented below, and the final product was identified as cotarnic acid. Nitromyristicinic acid must therefore possess the constitution I, and is 6-nitro-5-methoxy-3 : 4-methylenedioxybenzoic acid:



(I.) (III.) (IV.) (V.) (VI.)

The determination of the position of the nitro-group in nitromyristicinic acid establishes, in addition, the constitutions of nitromyristicinaldehyde (*loc. cit.*, p. 1160), and of a series of synthetic products derived from the latter compound * (Trans., 1909, **95**, 1204).

Experimental.

For the purpose of this investigation it was necessary to prepare a considerable quantity of nitromyristicinic acid. The method already described for the preparation of this compound (Trans., 1909, **95**, 1165) is unsatisfactory, since approximately 60 per cent. of the myristicinic acid is converted into 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene by elimination of carbon dioxide. It has now been found, however, that by esterification of the myristicinic acid prior to nitration the secondary change is entirely avoided.

* These compounds comprise: ω-2-dinitro-3-methoxy-4 : 5-methylenedioxystyrene; 2-nitro-3-methoxy-4 : 5-methylenedioxycinnamic acid; 2-amino-3-methoxy-4 : 5-methylenedioxycinnamic acid; 2-keto-8-methoxy-6 : 7-methylenedioxy-1 : 2-dihydroquinoline; 8-methoxy-6 : 7-methylenedioxycarbostyril methyl ether; 2-keto-8-methoxy-1-methyl-6 : 7-methylenedioxy-1 : 2-dihydroquinoline and oxy*iso*cotarnine.

Ethyl Nitromyristicinate (*Ethyl 2-Nitro-3-methoxy-4 : 5-methylenedioxybenzoate*), III, p. 267.

Twenty grams of ethyl myristicinate (b. p. 193°/20 mm.) were added gradually at 0° to 200 c.c. of concentrated nitric acid (D 1·41). The mixture was kept in the cold for an hour, and then poured into ice-water, when an oil was precipitated, which gradually solidified. This was collected, washed free from nitric acid, and purified by recrystallisation from alcohol. The compound was thus obtained in stout, colourless prisms, melting at 82°:

0·4019 required for saponification 15·05 c.c. *N*/10-NaOH. Saponification value = 210·1.

$C_{11}H_{11}O_7N$ requires saponification value = 208·6.

Ethyl nitromyristicinate is colourless when freshly prepared, but gradually becomes yellow on exposure to light. When hydrolysed, it yield a mononitromyristicinic acid, which was proved to be identical with the acid derived by the direct nitration of myristicinic acid.

Ethyl Aminomyristicinate (*Ethyl 2-Amino-3-methoxy-4 : 5-methylenedioxybenzoate*), IV, p. 267.

For the preparation of this compound, one part of ethyl nitromyristicinate was cautiously heated with tin (one part) and an excess of concentrated hydrochloric acid. After the vigorous reaction had subsided and the nitro-ester had completely dissolved, the mixture was poured into a large volume of water, when the greater portion of the amino-ester was precipitated as an oil, which soon became solid. This was collected, washed, and purified by recrystallisation from alcohol. A further quantity of the amino-ester was obtained from the acid filtrate by rendering it alkaline and extracting with ether:

0·1114 gave 0·2250 CO_2 and 0·0546 H_2O. C = 55·1; H = 5·4.

$C_{11}H_{13}O_5N$ requires C = 55·2; H = 5·4 per cent.

Ethyl aminomyristicinate crystallises from alcohol in colourless, prismatic needles, melting at 93°. Its ethereal solution possesses a blue fluorescence. It is a very weak base, being precipitated from its solution in concentrated hydrochloric acid by the addition of water. When hydrolysed, it yields aminomyristicinic acid, which crystallises from alcohol in long, slender, colourless needles, melting and decomposing at 200°. Solutions of the latter substance also show a blue fluorescence:

0·1190 gave 0·2239 CO_2 and 0·0480 H_2O. C = 51·3; H = 4·5.

$C_9H_9O_5N$ requires C = 51·2; H = 4·3 per cent.

Ethyl Cyanomyristicinate (*Ethyl 2-Cyano-3-methoxy-4 : 5-methylenedioxybenzoate*), V, p. 267.

Ethyl aminomyristicinate was dissolved in rather more than two molecular proportions of hot sulphuric acid (10 per cent.), and the solution cooled, with vigorous agitation. A solution of sodium nitrite (1 mol.) was slowly added at 0°. After some time the mixture was filtered to remove unchanged amino-ester, and the filtrate added in small portions to a hot solution of cuprous cyanide. The mixture was heated on the boiling-water bath for an hour, then cooled, and extracted with ether. The ethereal extract was washed first with sodium hydroxide, which removed some resinous matter, and then with water. On removing the solvent, the residue soon solidified; it was purified by crystallisation from alcohol, and thus obtained in yellow prisms, melting at 111°:

0·1252 gave 0·2652 CO_2 and 0·0534 H_2O. C = 57·8; H = 4·7.

$C_{10}H_7O_3N$ requires C = 57·8; H = 4·4 per cent.

Ethyl cyanomyristicinate is readily soluble in benzene, chloroform, or ether, but only moderately so in cold alcohol. When heated for a short time with alcoholic potassium hydroxide, it is converted into *cyanomyristicinic acid*, which crystallises from alcohol in prismatic needles, melting at 221°.

Cotarnic Acid, VI, p. 267.

In order to prepare cotarnic acid from ethyl cyanomyristicinate, the latter was heated with an excess of alcoholic potassium hydroxide until ammonia ceased to be evolved. After removing the alcohol, the alkaline liquid was acidified with dilute hydrochloric acid, and then extracted with ether. The ethereal solution yielded a crystalline residue, which was recrystallised from benzene containing a little methyl alcohol. It was thus obtained in colourless, square prisms, decomposing at 178° with the formation of an anhydride, which then melted at 160° (0·0990 required 8·25 c.c. *N*/10-KOH for neutralisation. M.W. = 240. $C_8H_6O_3(CO_2H)_2$ requires M.W. = 240).

It is evident that the above substance possesses the composition and properties of cotarnic acid. Its identity was further confirmed by conversion into the methylimide of cotarnic acid. This was prepared by dissolving the cotarnic acid in an excess of methylamine solution, evaporating to dryness, and subjecting the methylamine salt to destructive distillation under diminished pressure (compare Perkin, Robinson, and Thomas, Trans., 1909, **95**, 1984). The distillate solidified at once, and on recrystallisation from alcohol was

obtained in colourless needles. When heated in a capillary tube, the methylimide began to change about 186°, and completely melted at 199° with partial volatilisation. (Found, C = 56·5; H = 4·1. Calc., C = 56·2; H = 3·8 per cent.)

For purposes of comparison, a specimen of the methylimide of cotarnic acid was prepared by the oxidation of cotarnine (Freund and Wulff, *Ber.*, 1902, **35**, 1739). This product also began to change at about 186°, and melted completely at 199°, whilst admixture with the synthetic methylimide produced no change in the point of fusion. Freund and Wulff * (*loc. cit.*) attribute to the methylimide of cotarnic acid a melting point of 205—206°, but the present author, as seen above, has not been able to confirm this observation.

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* Since writing the above the author has received a private communication from Dr. M. Freund stating that the melting point previously ascribed to the methylimide of cotarnic acid is incorrect. A specimen of this substance kindly sent by Dr. Freund, to whom the author desires to express his sincere thanks, melted at 199° and was identical with the compound described in this investigation.

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